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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/754,723	01/04/2001	Ole Kirk	3745.234 US	3358

23650 7590 01/05/2006

NOVO NORDISK, INC.
PATENT DEPARTMENT
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PRINCETON, NJ 08540

EXAMINER

DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 01/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/754,723	KIRK, OLE	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10-3-05 has been entered.

The amendment filed 10-3-05 has been entered into the record. Claims 1-14 have been cancelled. Claims 15-32 are pending and under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Withdrawn

The rejection of claims 15-21, 23 and 24 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn based on Applicants amendments.

The rejection of claims 22 and 30-32 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn based on Applicants amendments.

Rejections Maintained

Claims 15-32 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Buckley et al (WO 91/11457) in view and Gutniak et al (Diabetologia, 33(suppl):A73, Abstract 246, 1990) of Ramachandran et al (Diabete Metabolisme, 13(2):140-141, 1987) Del Prato et al (The American Journal of Medicine, 90(suppl 6A):6A-77S, 1991) and Parker et al (Diabetes, Volume 40, Suppl 1, Abstract 847) is maintained for all reasons made of record and those herein.

Applicants' arguments have been carefully considered but are not persuasive.

Applicants acknowledge that Parker et al teaches motivation for the combination of the GLP-1 peptides and oral hypoglycemic agents to increase insulin secretion. Applicant argues that the generic teaching for oral hypoglycemic agents does not point one to metformin. This is not persuasive, metformin was and is a well known oral hypoglycemic agent at the time of the invention. The teaching is not overly broad, it specifically points to oral agents and the art of record recognizes that metformin is one of these oral hypoglycaemic agents. The genus of oral hypoglycemic agents is not overly broad and was restricted to a handful of drugs at the time that the invention was made. Applicants argue that not all oral hypoglycemic agents are alike and that the general teaching is insufficient on any further direction on how to proceed combining the two drugs renders the combination insufficient. This is not persuasive, the art of record already has multiple instances of the combination of oral hypoglycemic agents with other agents for the treatment of diabetes. Since both drugs are effective *in vivo* to treat an aspect of diabetes, the combination would reasonably be expected to be effective. Applicants also argue that Ramachandran et al provides no motivation. The relied upon teachings of Ramachandran et al are "... the combination of the oral hypoglycemic agents glibenclamide and metformin is effective in the treatment of Type II diabetes (see paragraph bridging pages 140-141)". The motivation articulated in the rejection of record was "... because Parker et al teach that the GLP-1 and glibenclamide when combined had an additive effect on the amount of insulin secretion and therefore the combination of the agents would be reasonably expected to be useful in the treatment of Type II diabetes. One would have been further motivated to combine the GLP-1 with metformin and glibenclamide because Del Prato teach that Type II diabetes is a heterogeneous disorder characterized by relative insulin deficiency and impaired insulin action and the combination of GLP-1 with the oral hypoglycemic agents would be reasonably expected to further increase the endogenous insulin levels and therefore be useful in the treatment of Type II diabetes and further, one skilled in the

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art would have a reasonable expectation of success because Gutniak et al that demonstrates that the *in vitro* pharmacology of GLP-1 correlates with the *in vivo* actions." Ramachandran et al was not relied upon for explicit motivation by the examiner in the combination as set forth in the art rejection of record in the office action mailed 12-12-03. Applicants argue that the study of Ramachandran et al were not controlled and therefore not credible. Applicants statement of lack of credibility of a published teaching in Journal specializing in Diabetes is mere opinion and does not obviate the facts set forth in the published documents. Applicants have not presented any extrinsic evidence that the findings of the published article are in fact false and one of skill in the art at the time of filing could not rely upon the finding that metformin was effective in the treatment of Type II diabetes. Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See MPEP § 2129 and § 2144.03 for a discussion of admissions as prior art. The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). See MPEP § 716.01(c) for examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration. In the instance of the assertion of lack of credibility in view of the lack of controls, it is noted that this is an opinion as to the ultimate legal conclusion that is not factually supported. In fact, that the article was published in a Journal that directly deals with Diabetes (i.e. Diabete Metabolisme) would support credibility. Applicants have not provided any objective factual evidence to support their position. Applicants argue that the examiner has cited no Authority for the expectation that agents developed to alleviate immunogenic insulin resistance could be used successfully to treat Type 2 diabetes. This is not persuasive, both GLP-1 and metformin were known and used in the art as combined to treat

Type 2 diabetes. The examiner did not use the argued limitations for treatment of Type 2 diabetes. Further, at the time of the invention, metformin was used for thirty years for the treatment of Type 2 diabetes (see Campbell of record). Applicants argue that the combination requires the removal of the glibenclamide. This in fact is not true and is not the combination set forth in the office action of record. Applicants are directed to the statement of motivation reiterated *supra*. Applicants are misstating and missinterpreting the rejection and combination as set forth in the rejection of record. As such, Applicants arguments are not persuasive. Applicants are arguing some altered combination that was not set forth in the outstanding art rejection. Applicants argue that the examiner has suggested that the combination is not an obvious to try but "common sense". First, the record does not establish "common sense" as a means for motivation and the record never uses these terms. The record reflects that the combination of agents is *prima facie* obvious over the art for reasons made of record and the idea of combining them logically flows from the art as each being used in combination or alone for treatment of Type 2 diabetes. This conclusion is fully supported in existing judicial precedent already cited in the record *In re Kirkhoven* (205 USPQ 1069, CCPA 1980).

The rejection is maintained.

Status of Claims

All claims stand rejected.

Conclusion

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy
Patricia A. Duffy

Primary Examiner

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